REMARKS

This paper is being filed in response to the Office Action dated May 3, 2002. Claims 1-7 are pending. Applicants have amended the Specification and the Abstract. No new matter has been added by these amendments.

In accordance with 37 C.F.R. §1.121, Applicants have provided (1) accurate instructions to amend the Specification and Abstract, (2) replacement Specification and Abstract in clean form herein, and (3) another version of the amended Specification and Abstract marked up to show all the changes relative to the previous version, which appears on an attached page.

The Examiner has made minor objections to the Specification and Abstract of the application. In addition, claims 1-7 stand rejected under the first paragraph of 35 U.S.C. §112. By this response, Applicants amend the Specification and Abstract to satisfy the Examiner's objections and respectfully traverse the Examiner's rejections of claims 1-7 under the first paragraph of 35 U.S.C. §112 for the reasons set forth below.

I. Objections:

The Examiner has objected to certain typographical errors throughout the specification and has made recommendations for correcting these errors. In response, Applicants have amended the Specification to correct these errors and has noted the Examiner's recommendations in doing so.

In addition, the Examiner has objected to the Abstract of the Application as to form. Applicants have accordingly amended the Abstract to better conform with the proper format and language for an Abstract. No new matter has been added by the amendments to the Specification

and Abstract. Therefore, Applicants respectfully request that the Examiner's objections to the Specification and Abstract be withdrawn.

II. Rejections under the first paragraph of 35 U.S.C.§112

The Examiner has rejected Claims 1-7 under 35 U.S.C.§112, first paragraph for lack of enablement or as failing to meet the written description requirement. Specifically, the Examiner contends that the specification does not provide an adequate enabling written description for peptides of SEQ ID NOs. 7-18 and 25-75.

The Examiner contends that according to the specification, the peptides of SEQ ID NOs. 1-6 are internalizing peptides, which is commensurate with the specification. The Examiner alleges however that the exact function of the remaining peptides enumerated in the claims (SEC ID NOs: 7-18 and 25-75) is not known and that the identity of these peptides is therefore speculative. Furthermore, the Examiner contends that there are no working examples for these peptides. The Examiner concludes that while the sequences of the peptides are identified in the specification, it is not possible to speculate their function or utility from their sequences. In support for his contention, the Examiner then discusses the Wands factors to be considered when determining whether there is sufficient evidence to determine whether the disclosure satisfies the enablement requirement and whether any experimentation is "undue."

In Response, Applicants wish to point out that the specification not only provides a description of each peptide indicated as not enabled by the Examiner (i.e. the specification includes the actual sequences of these peptides; *see, e.g.* pages 19-23, 25, 30, originally filed claims 1, 8, 40, 46, 49, 51, and 57 and the Sequence Listing) but also provides working examples which demonstrate the function and utility of the peptides. Example 3 of the Specification,

which starts on page 55 specifically provides a working example for the internalization capabilities of SEQ ID NOs: 1-18 and 25-72. As described in Example 3, a phage display library was used comprising a peptide library linked to phage (peptide + cargo) as further described in Examples 1 and 2. This phage display library was then incubated with cells to determine whether any of the peptides had the capability of internalizing the phage. It was then determined that SEQ ID NOs: 1-18 and 25-72 were able to internalize the phage. Thus, Example 3 specifically provides both function and utility support for all these sequences. In addition, page 33, lines 7-19 specifically describes and provides a working example of the ability of SEQ ID NO:73 to internalize cargo, which is further illustrated by Figures 23 and 24. SEQ ID NO:74 and SEQ ID NO:75 include the internalizing portion found in SEQ ID NO:73. Applicants therefore assert that the specification is not only enabling for peptides 1-6, as alleged by the Examiner, but is also fully enabling for SEQ ID NOs: 7-18 and 25-75. Furthermore, Applicants wish to point out that the specification need only provide one specific utility for the peptides and it does and demonstrates far more than that.

In addition, the Examiner similarly has rejected claims 1-7 under 35 U.S.C. § 112, first paragraph based on an inadequate written description. The Examiner contends that the specification does not provide an adequate written description for peptides 7-18 and 25-75 because the function (properties) of the other claimed peptides is not described in the specification. For the reasons discussed above, Applicants assert that the function and properties of all the claimed peptides is set forth in the specification and that at least one utility is provided. Notwithstanding, Applicant wish to point out that the claims are directed to specific peptide sequences and a written description of the peptide sequences is provided several times throughout the specification. The Examiner states that the Federal Circuit requires that a

"written description of a chemical species requires a precise definition" and alleges that the Specification does not provide such a definition. The Examiner cites to *University of California v. Eli Lilly & Co.*, 43 U.S.P.Q.2d 1398, 1405 (1997), quoting *Fiers v. Revel*, 25 U.S.P.Q.2d 1601, 1606 (Fed. Cir. 1993). Applicants submit that the Federal Circuit in the *Lilly* case indicated that the precise definition for a DNA is its nucleotide sequence. The specification only taught certain sequences and therefore, the claims had to be limited to only those DNA sequences described in the specification. The claims were deemed to not comply with 35 U.S.C. § 112, first paragraph because the claims encompassed many other DNA sequences (*i.e.* any DNA sequence having the recited function) and accordingly the claims were not adequately described by the specification, which did not describe every such sequence. As pointed out by the Examiner, the claims of the patent in suit in *Lily* were directed to a genus of DNA sequences defined by their function, rather than by a specific sequence. The claims of the present application, in stark contrast and completely within the requirements set forth by *Lilly*, are directed to specific peptide sequences rather than a genus of every sequence having a particular function (*e.g.*, having internalization capabilities.) Therefore, Applicants respectfully request that the rejections under 35 U.S.C. § 112, first paragraph be withdrawn.

CONCLUSION

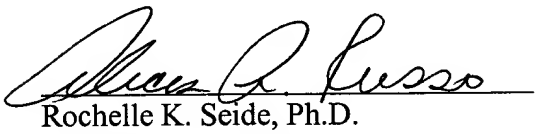
Based on the foregoing amendments and remarks, Applicants submit that the present application is in condition for allowance. A Notice of Allowance is therefore respectfully requested.

Applicants believe no fee is due with this Response. However, if any fee is due, the Commissioner is hereby authorized to charge Deposit Account Number 02-4377. A duplicate copy of this communication is enclosed.

If a telephone interview would be of assistance in advancing the prosecution of the subject application, Applicant's undersigned attorney invites the Examiner to telephone at the number provided below.

Respectfully submitted,

BAKER BOTTS L.L.P.



Rochelle K. Seide, Ph.D.
PTO Reg. No. 32,300

Alicia A. Russo
PTO Registration No. 46,192

Attorneys for Applicant(s)
(212) 408-2627

VERSION WITH MARKINGS TO SHOW CHANGES

IN THE SPECIFICATION:

Please amend the specification by replacing the paragraph that begins on line 1 of page 11 with the following substitute paragraph:

fluorescent [flourescent] detection of eGFP); (D & E) shows the ability of peptide 5 to internalize eGFP in human islets at high magnification (D is a photomicrograph of the histologically [histollogical ly] stained cells and E shows the fluorescent [flourescent] detection of eGFP); and (F & G) shows the ability of peptide 5 to internalize eGFP in human dendritic cells (F is a photomicrograph of the histologically [histological ly] stained cells and G shows the fluorescent [flourescent] detection of eGFP).

Please amend the specification by replacing the paragraph that begins on line 3 of page 23 with the following substitute paragraph:

Of the peptides of Table 4, three have homology to known proteins. Pep63 (SEQ ID NO:69) is homologous to a bacterial protein methenyl tetrahydromethanopterin cyclohydrolase of xanthobacter autotrophicus (Genbank Accession Number AF139593). Pep65 (SEQ ID NO:71) is homologous to a yeast hypothetical protein in the MPP10-SAG1 intergenic region of Saccharomyces cerevisiae (Genbank Accession Number NP012536.1). Additionally,[_]pep66 (SEQ ID NO:72) is homologous to herpesvirus 1 [probably] nuclear antigen protein (Genbank Accession Number P33485).

Please amend the specification by replacing the paragraph that begins on line 17 of page 29 with the following substitute paragraph:

Rheumatoid arthritis (RA) is a chronic inflammatory disease which is characterized by hyperplasia of the synovial lining of cells, angiogenesis, and infiltration of mononuclear cells resulting in pannus formation, cartilage erosion and ultimately joint destruction. Most of articular cartilage consists of collagens and proteoglycans whose degradation is initiated extra- or peri- cellularly by proteinases produced locally by cells in [a] and

Please amend the specification by replacing the paragraph that begins on line 6 of page 60 with the following substitute paragraph:

Figure 6 A-I shows the ability of peptide 5 (SEQ ID NO:5) to facilitate the uptake of β-gal in (6A) HIG-82 cells; (6B) rabbit primary synovial cells; (6C) human primary synovial cells; (6D) HBE 144 primary human airway epithelial cells; (6E) MDCK polarized canine kidney cells ; (6F) human β islet primary cells; (6G) C2C12 murine myoblast cells; (6H) MCA205 murine fibrosarcoma cells; and (6I) NIH3T3 cells. Additionally, Figure 9B-C shows the ability of peptide 5 to facilitate internalization of eGFP in human islets at low magnification (9B is a photomicrograph of the histologically [histological ly] stained cells and 9C shows the fluorescent [flourescent] detection of eGFP). Figure 9D-E show the ability of peptide 5 to facilitate internalization eGFP in human islets at high magnification (9D is a photomicrograph of the histologically [histological ly] stained cells and 9E shows the fluorescent [flourescent] detection of eGFP). Figure 9F-G shows the ability of peptide 5 to facilitate the internalization of eGFP in human dendritic cells (9F is a photomicrograph of the histologically [histological ly] stained cells and 9G shows the fluorescent [flourescent] detection of eGFP). Figure 9A is a schematic representation of the expression construct encoding the peptide5-eGFP fusion protein.

In the Abstract:

Please amend the Abstract as follows:

ABSTRACT

The present invention relates to internalizing peptides which facilitate the uptake and transport of cargo into the cytoplasm and nuclei of cells as well as methods for the identification of [such] the peptides, and methods of use for the peptides. The internalizing peptides of the present invention are selected for their ability to efficiently internalize cargo into a wide variety of cell types both *in vivo* and *in vitro*. [The method for identification of the internalizing peptides of the present invention comprises incubating a target cell with a peptide display library, isolating peptides with internalization characteristics and determining the ability of said peptide to internalize cargo into a cell.]